



# Uterine Fibroids: An introduction

Shannon Laughlin-Tommaso, MD MPH  
Fibroid Center & Minimally Invasive Gynecologic Surgery  
Mayo Clinic, Rochester  
July 10-11, Silver Springs, MD

# Disclosures

- No financial disclosures or conflicts of interest
- Co-investigator, Clinical study to evaluate safety of ExAblate Model 2100 System for Symptomatic Uterine Fibroids
  - (Sponsored by InSightec)
- Co-investigator, FIRSTT trial (Comparing UAE and FUS)
- Co-investigator, Study of environment, lifestyle and fibroids

# Objectives

- Discuss the biology, epidemiology, and impact of fibroids
- Describe the clinical presentation and effects on quality of life
- Provide an overview of the medical and minimally invasive fibroids therapies

# What are fibroids?

- Benign smooth muscle cell tumor: “leiomyoma”
- Bulky fibrous physiologically active extracellular tissue (collagen): “fibroids”
- Arise from single cell & are monoclonal
  - But, a single uterus can have multiple independent tumors
- Most common reproductive tumor in women

# What are fibroids?

- Hormonally dependent
  - Menarche → menopause
  - Estrogen, progesterone and aromatase receptors in fibroid tissue
- Chromosomal abnormalities are common (40%)
  - Trisomy 12
  - T(12;14)
  - Deletions of 7q, 3q, 1p

# How do leiomyosarcomas differ?

- Rare, fatal tumors with 4 histologic patterns:
  - Nuclear atypia
  - Mitotic activity
  - Necrosis
  - High cellularity
- Fibroid variants may have one of the above but not all
  - Usually benign course

# Fibroids grow at different rates

- Fibroids in same uterus grow (or shrink) at different rates
- Range of growth: -89% to +138% in 6 months (median +9%)
- For black women: growth continued at same rate up to menopause
  - For white women: growth rate slowed after age 45

Peddada et al, PNAS, 2008

# Fibroid are common

- Symptomatic fibroids: estimated 25%
- Pathology specimens: ~80%
- Ultrasound-screening studies: up to 80% by age 50
- Incidence differs between white and black women
  - Studies of self-reported fibroids: 9 (white) - 34 (Black)/1000 woman-yrs

Cramer and Patel 1990; Marshall et al 1997;  
Wise et al, 2006; Baird et al, 2003



# Public Health Impact of Fibroids

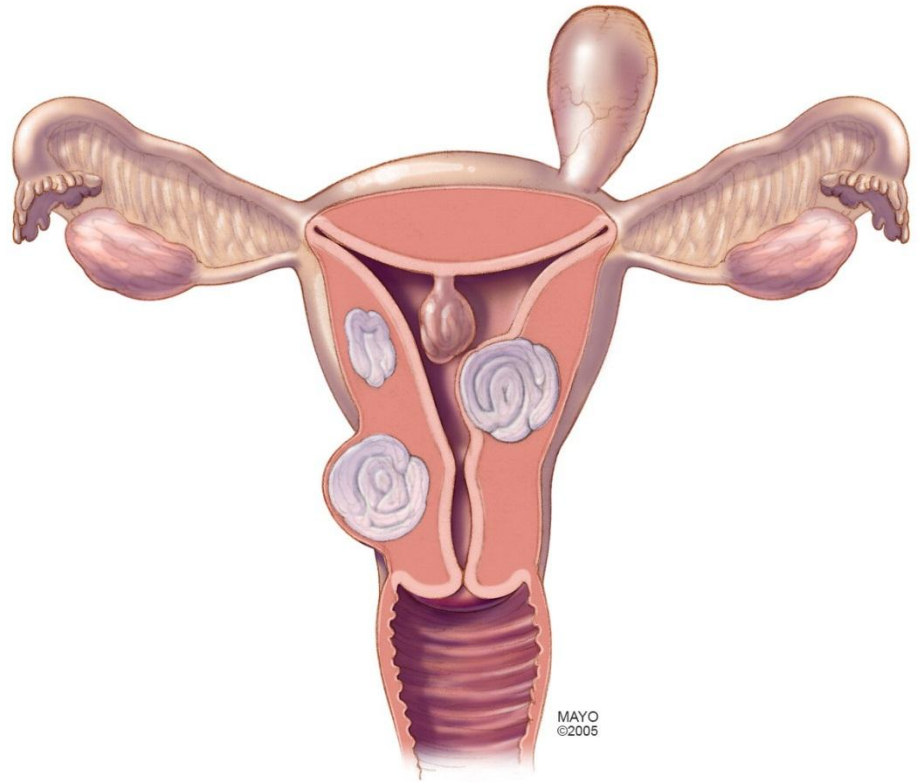
- 400,000 new cases per year<sup>1</sup>
- Myomectomy
  - >30,000 per year in US
  - Direct & indirect costs: \$30,206-\$39,207<sup>2</sup>
- Hysterectomy
  - 600,000 per year in US
  - 40% for fibroids
  - Direct & indirect costs: \$31,559- \$42,619<sup>2</sup>
  - Health disparity: black>>white women<sup>3,4</sup>

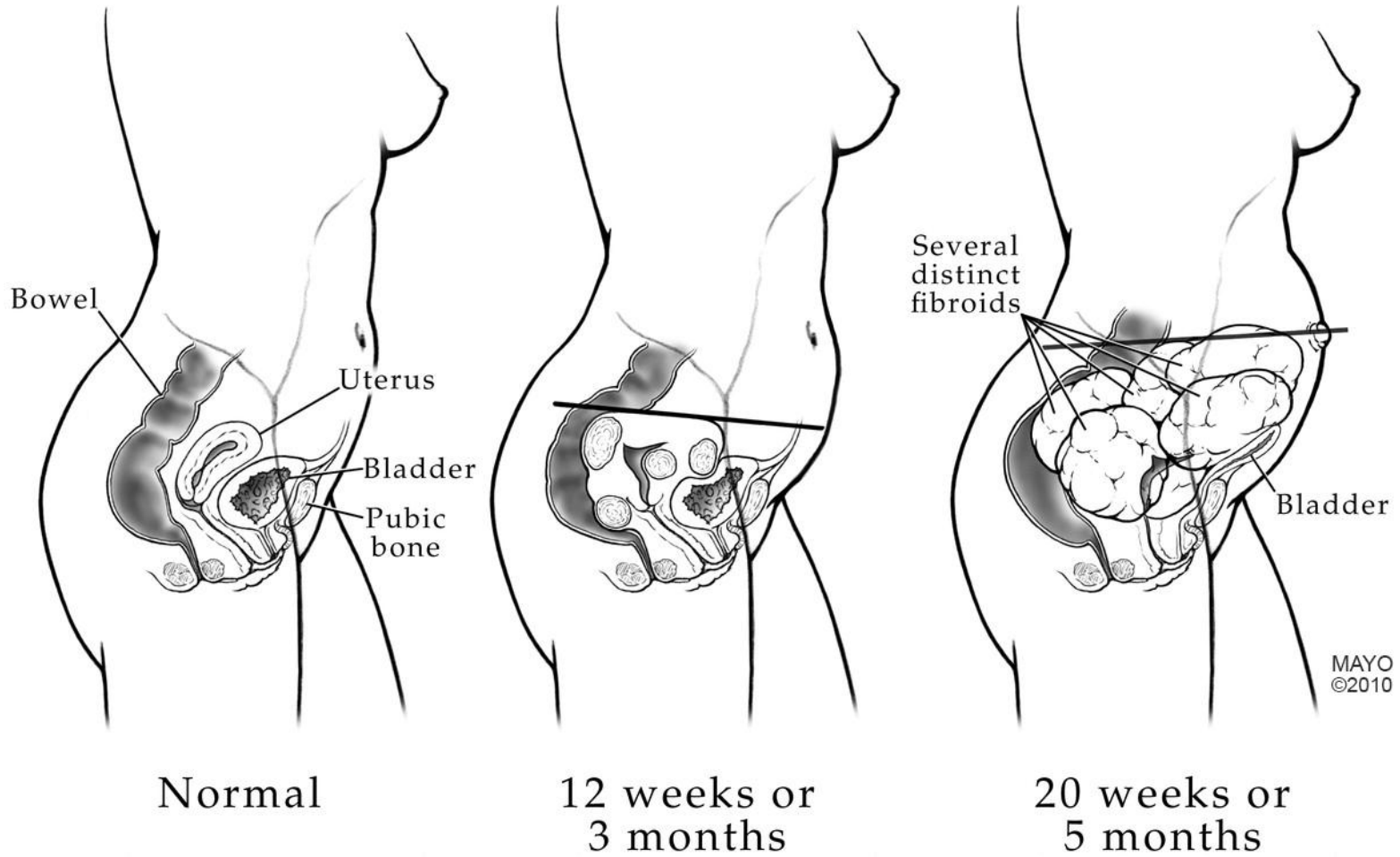
<sup>1</sup>Hartmann et al, 2006, <sup>2</sup>Carls et al, 2008; <sup>3</sup>Viswanathan, 2007

<sup>4</sup>Eltoukhi et al, 2013

# How do women present clinically?

- Menstrual cramps and pain
- Heavy menstrual bleeding & anemia
- Problems with fertility or pregnancy
- Bladder or bowel symptoms





Fibroid size compared to pregnancy weeks

# Black women are disproportionately affected

- More symptoms
  - 40% report menstrual pain and cramps
  - 3-fold increased risk of anemia
- 2.4x risk of hysterectomy
- Nearly 7-fold risk of myomectomy
- Higher uterine weights
- More fibroids & larger volume

Eltoukhi et al, 2013, Wechter et al, 2011

# Fibroids affect quality of life

- Relationship impacts:
  - 14% childcare, 15% friends, 22% partner
- Work:
  - 29% missed work days
  - 24% reported lost potential
  - 27% unable to do part of their job
  - 12% feared losing their job
  - 15% could not travel

Stewart et al, 2013

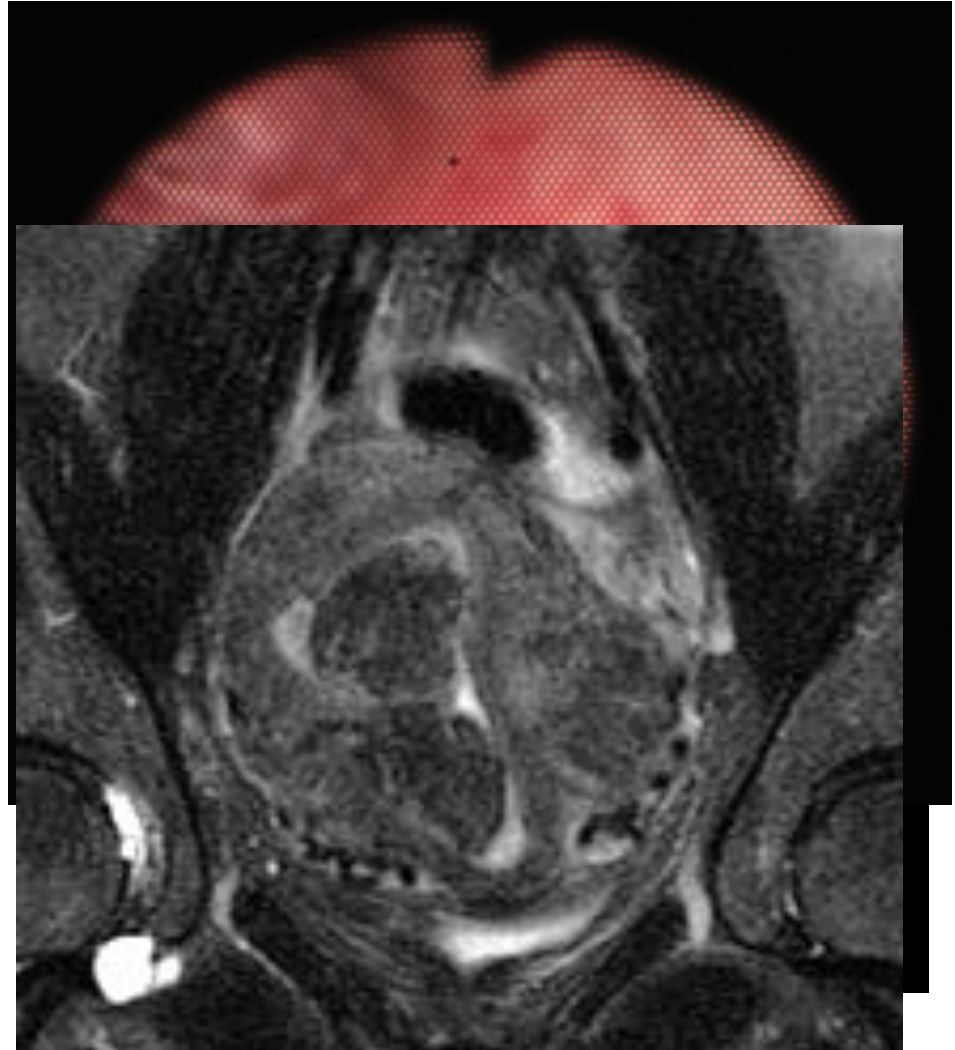
# Fibroids affect quality of life

- Fears about fibroids:
  - 77% growth
  - 53% cancer
  - 25% unable to become pregnant (twice as high in African American women than white)
- Concerns about treatments:
  - 81% invasiveness
  - 64% sexuality
- 49% wanted fertility sparing option (70% v. 30%)

Stewart et al, 2013

# Fibroid evaluation

- Pelvic exam
- Ultrasound
- Endometrial biopsy
- Blood counts
- Pelvic MRI
- ?Hysteroscopy



# When do we treat fibroids?

- Fibroids that are symptomatic at any age can be treated
  - Imaging will help
- Options: treat symptoms vs. treating fibroids
- Fertility issues:
  - Submucosal fibroids
  - Intramural fibroids >5 cm
  - Treatments that optimize future fertility:
    - MRgFUS
    - Myomectomy

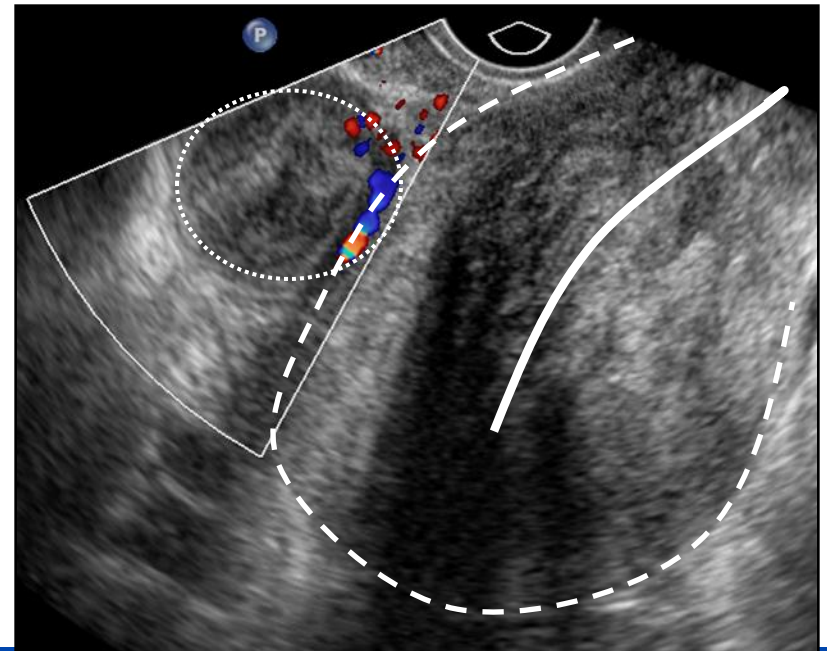


## When do we not treat fibroids?

- Asymptomatic or an incidental finding
- Rapid growth without symptoms
- Postmenopausal\*

# Treatment options for bleeding

- NSAIDs
- Tranexamic acid
- Contraceptive hormones (estrogen-progestin or progestin alone)
- Mirena IUD
- Endometrial ablation

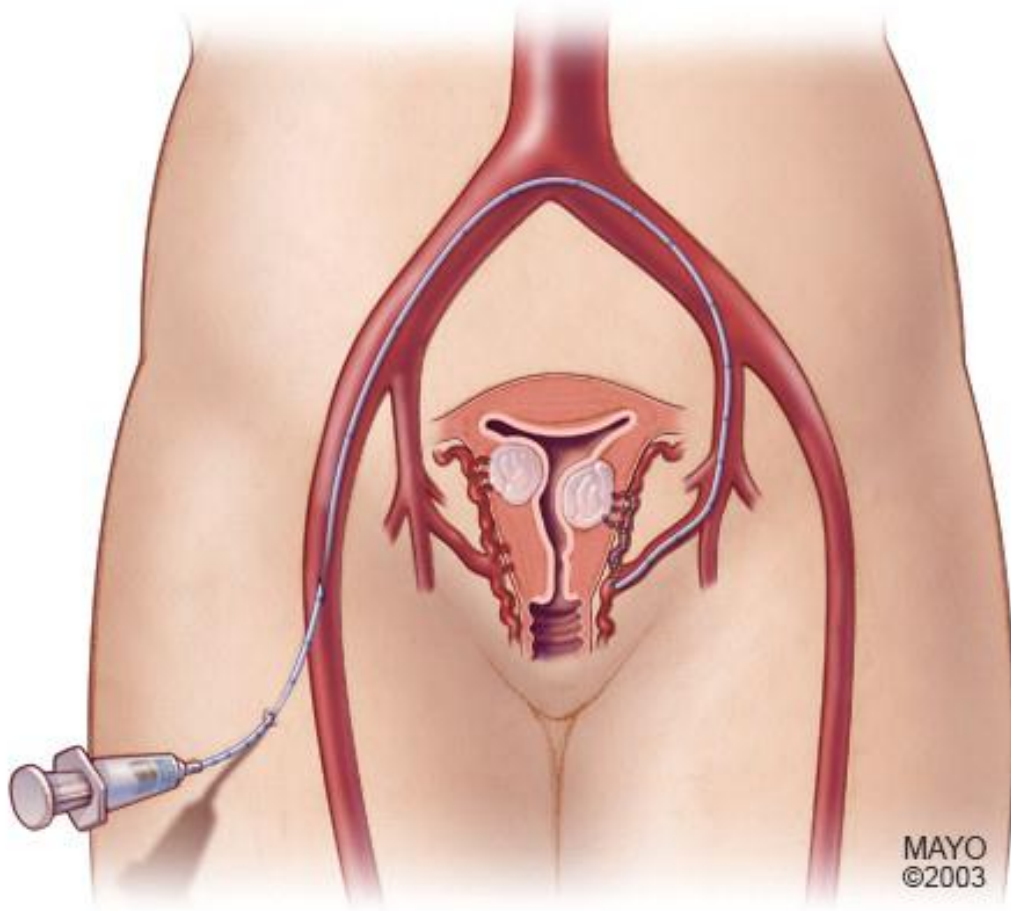


# Medical options for fibroids and bleeding

- Leuprolide acetate:
  - GnRH agonists/antagonists
  - Controls bleeding
  - Shrinks fibroids
- Ulipristal acetate:
  - Selective progesterone-receptor modulator
  - Controls bleeding in >90% of women
  - Shrinks fibroids
  - Not available for use in US currently

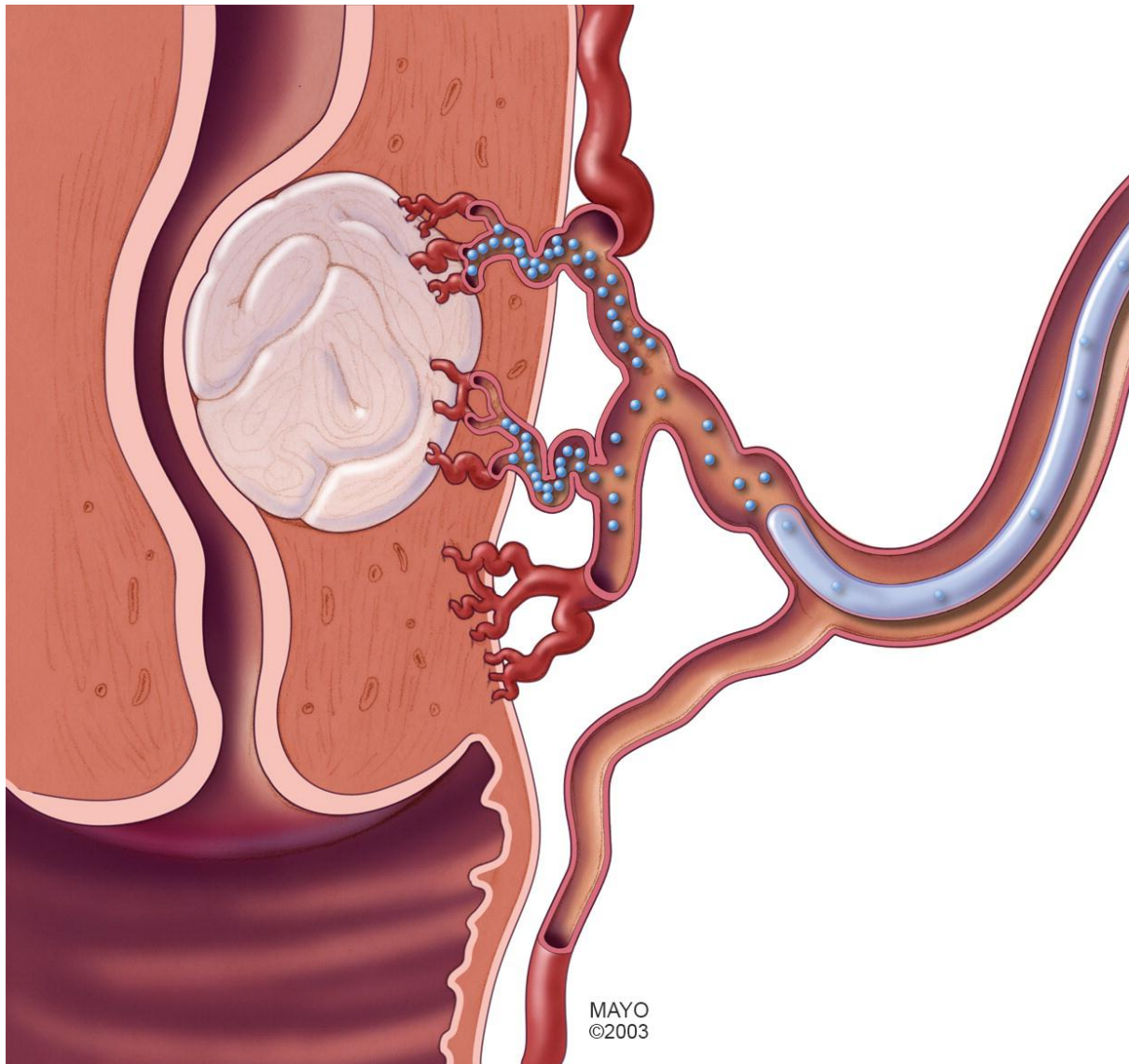
# Minimally Invasive Treatments

# Uterine Artery Embolization



## UAE: how it works

- Catheter placed in common femoral artery
- Travels through anterior internal iliac to uterine arteries
- Position confirmed with angiography
- Embolic agents (polyvinyl alcohol particles)
- Compression on incision to reduce hematoma



MAYO  
©2003

## UAE: Candidates

- UAE has a more global treatment
- Relative cut-off of 10 cm
- No active genitourinary infection/ malignancy
- No severe vascular disease (limits vessel access)
- No iodine contrast allergy
- Good renal function
- Hysteroscopically resectable SM fibroids



# UAE: Details

- 2-3 hour procedure under fluoroscopy
- Overnight stay for pain control
- Incision in groin

## UAE: risks

- Amenorrhea: 3% if <40yrs, 40% if >50 yrs
- Markers of ovarian reserve have shown lower ovarian function after UAE compared with myomectomy
  - Also found with hysterectomy
- Postembolization syndrome: pain, nausea, vomiting, leukocytosis, malaise

# Symptom Relief from UAE

- Menorrhagia: 83% improved
- Dysmenorrhea: 77% improved
- Urinary frequency: 86% improved
- 91% satisfaction
- Fibroid volume reduced 42% at 3 months
  - Symptoms unrelated to volume reduction

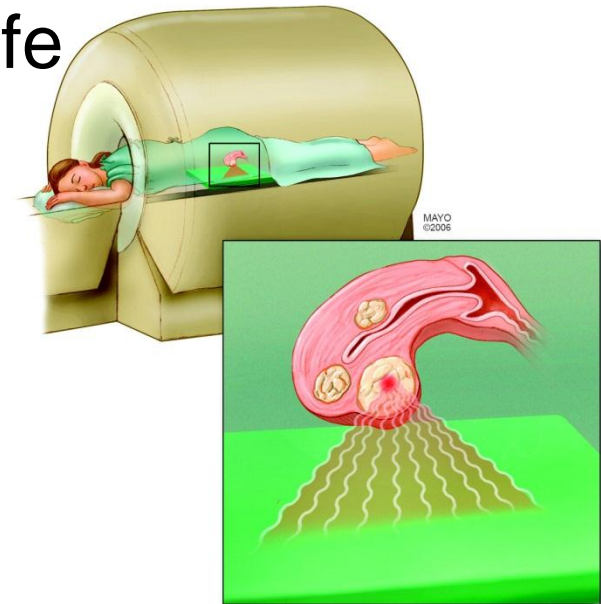
# Pregnancies after UAE

- 164/555 desired fertility (? 35 trying at 1 year)
  - 24 pregnancies
  - 18 live births – 4 preterm
  - 3 abnormal placentations
- 23/102 desired fertility
  - 61% pregnancy rate
  - 2 miscarriages
  - 13 went to term without complication

Pron et al, Obstet Gynecol, 2005; Firouznia et al, AJR, 2009

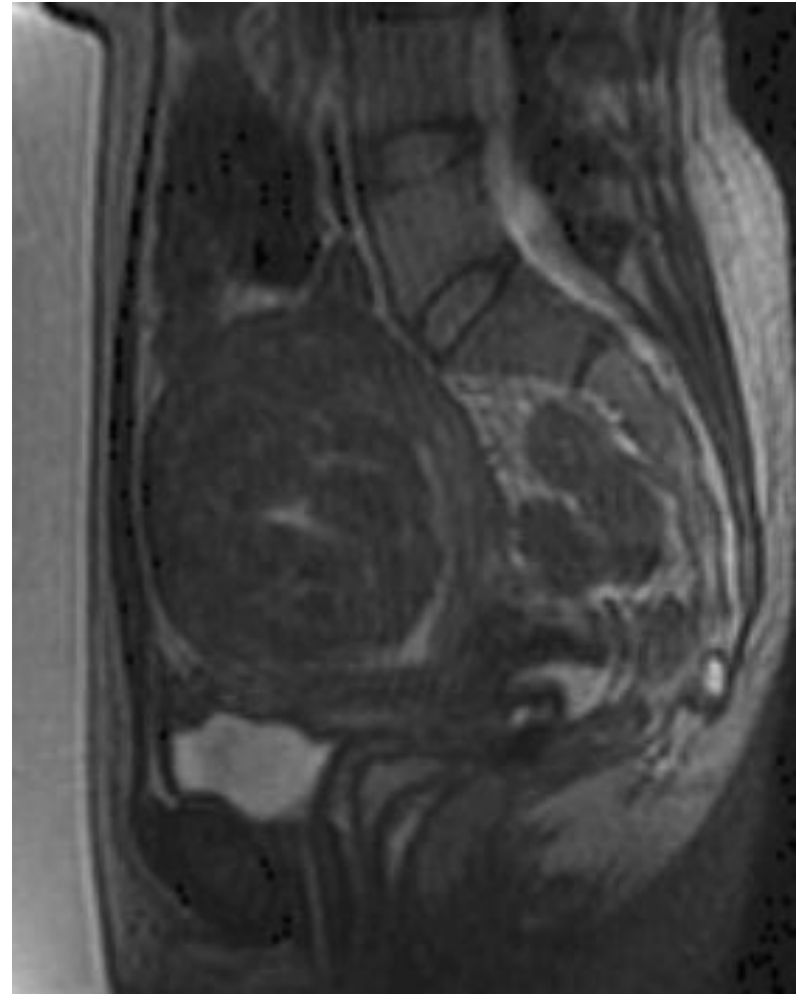
# MRgFUS: how it works

- FDA approved in 2004
- Focused ultrasound beam
  - Temperature highest in focal spot
  - Non-target areas relatively safe
- MRI:
  - Mapping of fibroids & beam guidance
  - Thermal monitoring
  - Treatment effect



# MRgFUS: Candidates?

- Few large fibroids
- Accessible by FUS
- Relative cut-off at 10 cm in diameter
- No metal or scars
- Good renal function due to Gadolinium use



# MRgFUS: Details

- ~3 hour treatment, possible 2 days in a row
- Done under IV sedation/pain medications and with urinary catheter
- Outpatient (goes home same day)
- Requires minimal pain medication prescriptions
- No incisions/ no radiation



Uterine fibroid



Treated (dead) tissue



Fibroid before treatment (left image). Treated fibroid (right image).

MAYO  
©2012



# MRgFUS: Risks

- Skin burns: resolved with procedural changes
- Inflammation of subcutaneous fat and muscle
  - Mainly asymptomatic
- Bowel injury
- Paresthesias:
  - Sonicate 4cm from bony structures
  - Generally spontaneously resolve

Hesley et al. Ultrasound Q, 2008

# Symptom relief from MRgFUS

- Symptoms lowest at 3 months
  - Symptom severity score dropped by 50%
  - 91% have symptom relief at 12 months
- Probability of another procedure:
  - The more volume you treat, the better the outcome
  - ~20% at 2 years with 50% treated
  - ~20% at 4 years with unrestricted treatment

Stewart et al. Obstet Gynecol 2007  
Fennessy et al. Radiology 2007

# MRgFUS: fertility-sparing option

- Observational studies only
- 54 pregnancies
  - 51% delivered at term, 33% miscarried
  - High vaginal delivery rate
  - No distinct patterns of complications
- Success with *in vitro* fertilization after MRgFUS
- Counsel women on the risks that are known and unknown

Rabinovici, Fertil Steril, 2010

# Summary

- Fibroids are common and costly
- African-American women are disproportionately affected
- Symptomatic fibroids can be treated, asymptomatic fibroids can be left alone
- There are many alternatives to hysterectomy that are durable and effective

# Questions?